

## REMARKS

### I. Generally

By this amendment, Claims 1, 3-5, 10, and 12-17 are cancelled. Claims 2, 6, 8, and 11 have been amended. Claims 18-24 have been added. In accordance with the requirements of the restriction and the May 21, 2003 office action, the claims have been narrowed to the method of using only neomycin to bind to RNA-DNA hybrid substrates, which then prevents reverse transcriptase (RT) from cleaving the RNA strand of the hybrid substrate. Ultimately, this method prevents a virus using reverse transcriptase from replicating.

### II. Rejection under 112(2)

The Office Action rejects the pending claims under 112(2) for being indefinite. The present amendments have addressed the four rejections listed on page 2 of the May 21, 2003 office action, either because the claims have been amended or have been cancelled.

### III. Rejection under 103(a)

The Office Action then rejects the pending claims under 103(a) as being obvious over: (a) Coffee in view of Furfine and Hammer and (b) Green. Applicants respectfully traverse these rejections to the extent that they are not overcome by the present claim amendments.

(a) Coffee in view of Furfine and Hammer

The pending claims are now directed to a method of using neomycin to bind an RNA-DNA hybrid structure, which prevents RT from cleaving the RNA strand of the RNA-DNA hybrid substrate. If this function does not occur during reverse transcription, the RNA strand remains attached to the DNA. Thus, the reverse transcription process is stalled.

Coffee, et al. (CAPLUS Abstract, AN 2001:637204, 2001) teach using aminoglycosides, including neomycin, to stabilize triple helical structures. Coffee limits their findings to triple helical structures and specifically points out the virtue of neomycin as a “triplex selective stabilization agent.” Coffee does not teach or suggest using the neomycin to bind to the RNA-DNA duplexes to block the RNase H activity of RT. Further, the present invention is directed to the RNA-DNA duplex (two-stranded) and not to a triple helical (three-stranded) structure. The newly limited claims, directed to a method of suppressing RNase H activity of RT, further illustrate the differences between the present invention and Coffee. Thus, it would not have been prima facie obvious to combine Coffee with any other reference to achieve the present invention.

The Office Action cites two references for the obviousness combination: Furfine et al. (“Human Immunodeficiency Virus Reverse Transcriptase Ribonuclease H: Specificity of the tRNA<sup>Lys3</sup>-Primer Excision,” *Biochemistry*, Vol. 30, No. 29, 7041-7046, 1991) and Hammer (“Advances in antiretroviral therapy and viral load monitoring,” *AIDS*, Vol. 10, Suppl. 3, S1-S11, 1996). The Office Action states on page 4 that it “would have been prima facie obvious to employ the method to suppress HIV reverse transcriptase because it is a known method to suppress HIV.”

Furfine is a 1991 article that describes two model substrates prepared to examine the mechanism of tRNA-primer excision catalyzed by RT-RNase H. Furfine describes some of the early discoveries relating to the functioning of RNase H, but in no way teaches or suggests using neomycin, or any compound for that matter, to control the functioning of RT. Furfine targets the enzyme (RNase H), whereas the present invention targets the substrate (RNA-DNA duplex). Therefore, the citation of Furfine is inapposite.

Hammer, a summary article from 1996 on pages S4-S5, describes non-nucleoside RT inhibitors as antiretroviral agents. These agents include nevirapine, delavirdine, loviride, and DMP-266. While Hammer talks about these compounds as a way to inhibit RT in HIV, it does not teach or suggest anything about using an aminoglycoside, particularly neomycin, to bind to RNA. Thus, Coffee in combination with either Furfine or Hammer does not teach or suggest the method of the present invention. Applicants respectfully request that this rejection be withdrawn.

(b) Green

The second obviousness rejection is a 103(a) rejection over Green (USPN 5534408) alone. Green discloses a method of using 2-DOS aminoglycosides, including neomycin B, to bind to a Rev-responsive element (See Abstract). Rev acts posttranslationally to increase cytoplasmic accumulation of viral gag, pol, and env messenger RNAs. In contrast, the mechanism of the present invention uses neomycin to inhibit the RNase H function of RT during reverse transcription. Significantly, this process occurs much earlier in the viral life cycle than the interaction studied by Green. The amended claims now clearly show that the

known molecule, neomycin, is being used for a different purpose, which is to substantially bind to the RNA-DNA substrate and to prevent RT from cleaving RNA. Given the amendments and remarks above, Applicants request that this obviousness rejection also be withdrawn.

**CONCLUSION**

The Commissioner is authorized to charge any fees required by the filing of these papers, and to credit any overpayment to Perkins Coie's Deposit Account No. **50-2586**. If anything can be done to further this application, please contact the undersigned at 310-788-9900.

Respectfully submitted,

PERKINS COIE LLP

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By: 

Lauren Sliger  
Reg. No. 51,086

**Correspondence Address:**

Customer No. 34055  
Perkins Coie LLP  
P.O. Box 1208  
Seattle, WA 98111-1208  
Ph: (310) 788-9900  
Fax: (310) 788-3399